REMARKS

Applicant filed a response to the final Office Action of July 21, 2010 on September 21, 2010. The Examiner issued an Advisory Action on October 12, 2010 in which she withdrew the outstanding § 102 rejection but maintained the § 103 rejection. Applicant subsequently filed a Request for Continued Examination (RCE) on October 21, 2010. Herewith Applicant files an Amendment to be entered and considered prior to continued examination of this case.

Claims 1-7, 11-12, 15-21, 35-37, 39, 41, 43, 45, and 49 were pending in the Application before entrance of this Amendment. Claims 36-37, 41, 43, and 45 have been withdrawn from consideration by the Examiner at this time. Claims 1-2, 11-12, 15-19, and 35 are amended by the present Amendment. No claims have been canceled, and no new claims have been added. Thus, claims 1-7, 11-12, 15-21, 35-37, 39, 41, 43, 45, and 49 are pending, and of these, claims 1-7, 11-12, 15-21, 35, and 49 are under consideration by the Examiner.

Claim amendments

Claims 1 and 35 have been amended to specify that the formulation "is contained in a nasal spray device." Support for this amendment is found on page 5, line 17, of the Application as originally filed.

Claims 2, 11-12, 15-19, and 35, have been amended to specify that the immune response modifier also includes "pharmaceutically acceptable salts thereof." Support for this amendment is found on page 81, lines 16-17, 22, and 25, and original claims 20-21, of the Application as originally filed.

Applicant submits that no new matter has been added to this Application by the present Amendment.

Rejection under 35 U.S.C. § 103(a)

The Examiner maintained the rejection of previous claims 1-7, 11, 12, 15-21, 35, and 49, under 35 U.S.C. § 103(a) as obvious over U.S. Patents 6,331,539 (hereafter "Crooks") and 6,083,505 (hereafter "Miller") in view of U.S. Patent 6,245,776 (hereafter "Skwierczynski").

Independent claims 1 and 35, as currently amended, are directed to aqueous sprayable formulations comprising an immune response modifier, water, and a hydrophilic viscosity enhancing agent, wherein the formulation is a solution at room temperature, has a viscosity of less than 100 cps at room temperature, and is contained in a nasal spray device. Claim 5, dependent on claim 1, defines the hydrophilic viscosity enhancing agent as selected from group consisting of cellulose ethers, polysaccharide gums, and acrylic acid polymers. Claim 7 defines the hydrophilic viscosity enhancing agent as selected from the group consisting of an acrylic acid polymer, carboxymethyl cellulose sodium, and xanthan gum.

The Examiner acknowledges that neither Crooks, Miller, nor Skwierczynski teach formulations having a viscosity of less than 100 cps. The Examiner also acknowledges that neither Crooks, Miller, nor Skwierczynski teach sprayable formulations. However, despite these deficiencies in the cited art, the Examiner has maintained the § 103 rejection of the previous claims over Crooks, Miller, and Skwierczynski since the Examiner finds that "viscosity" and "sprayable" are characteristic properties of the compositions taught therein. In particular, the Examiner finds that Miller teaches a composition comprising an immune response modifier, water, carriers, and polysaccharides, and that this composition is contemplated for nasal administration, and may be injected (column 3, lines 4-11; column 8, lines 13 and 61-67; column 9, lines 2, 5, and 41-42; and claims 1 and 7 of Miller). The Examiner posits that since the composition may be injected, the injectable composition is a solution and therefore also sprayable. The Examiner also finds Skwierczynski teaches use of 0.5% w/w xanthan gum in a composition containing an immune response modifier (column 18, Table 1, line 49, of Skwierczynski). Thus, the Examiner concludes that Crooks, Miller, and Skwierczynski render the instant claims obvious since the combination teaches a composition, comprising an immune response modifier, water, and a hydrophilic viscosity enhancing agent, which is injectable and capable of being sprayed. Applicant respectfully disagrees.

Crooks teaches immune response modifiers and pharmaceutical compositions thereof, wherein the composition contains the immune response modifier in combination with a pharmaceutically acceptable carrier, and may be provided in any conventional dosage form "such as tablets, lozenges, parenteral formulations, syrups, creams, ointments, aerosol formulations,

transdermal patches, transmucosal patches and the like" (column 14, lines 26-28 and 42-45, of Crooks). Crooks does not elaborate any further on the nature of the carrier, dosage form, or pharmaceutical composition containing the immune response modifier beyond this very general teaching.

Miller teaches pharmaceutical compositions containing an immune response modifier in combination with an immunogen and a pharmaceutically acceptable carrier (column 3, lines 4-8, of Miller). Miller defines "immunogen" as "any material that raises either humoral or cell mediated immune response, or both" and lists "polysaccharides" as an exemplary immunogen, but does not provide any specific examples of immunogens which are polysaccharides, let alone suggest that xanthan gum is an immunogen (column 8, lines 8-9 and 13, of Miller). Specifically, Miller teaches use of a polysaccharide as an active ingredient (*i.e.*, as an immunogen) rather than as an excipient (*i.e.*, a hydrophilic viscosity enhancing agent) as is presently claimed, and Miller does not teach that the immunogens may affect formulation viscosity.

As stated above, the Examiner finds that Miller teaches a composition which may be administered by injection (column 9, line 5, of Miller), and that this reference to "injection" in Miller teaches, by extension, that the composition is a solution and therefore sprayable. Applicant disagrees with this assumption. Viscous formulations can be injected but are not necessarily sprayable. In fact, the only "working" formulation of Miller that is topically administered is a viscous formulation, *i.e.*, a cream containing an immune response modifier, water, isosteric acid, stearyl alcohol, polysorbate 60, cetyl alcohol, benzyl alcohol, glycerin, sorbitan monostearate, methylparaben, and propylparaben, administered intravaginally to female guinea pigs (column 14, lines 37-43 and 56, of Miller). There is no indication that such a viscous formulation is sprayable, particularly from a nasal spray device. Additionally, this topical formulation also lacks the immunogen (*i.e.*, polysaccharide) recited by Miller (the immunogen is in fact administered separately).

Furthermore, the only "working" formulations of Miller that are actually injected are compositions of an immune response modifier in water administered intraperitoneally to mice (column 13, lines 25-27, of Miller) or subcutaneously to guinea pigs (column 14, lines 47-48). Such a composition may be able to be sprayed; however, it does not include a viscosity enhancing agent,

as required by Applicant's claims. In fact, Miller's injectable compositions also do not contain the immunogens (*i.e.*, polysaccharides) recited by Miller. Rather, the immunogen is administered separately from the injectable IRM formulation.

Skwierczynski does not remedy the deficiencies of Crooks or Miller. Skwierczynski, like Miller, teaches pharmaceutical compositions containing an immune response modifier for intravaginal administration, specifically to the cervical mucosa (column 17, line 22-23, of Skwierczynski). Skwierczynski teaches that, preferably, "the IRM [immune response modifier] is formulated to include a viscosity agent…to enhance the residence time of the IRM on the cervix" (column 17, lines 33-35, of Skwierczynski). Indeed, the only "working" formulations of Skwierczynski are formulations A-J of Examples 1-7 having high viscosity. Example 6 of Skwierczynski compares the pharmacokinetics of an immune response modifier in rats after a single dose vaginal application of Formulation A and Formulation B. Formulation A is a cream formulation containing all of the ingredients of the cream formulation disclosed in Miller (*i.e.*, containing the same immune response modifier, water, isosteric acid, stearyl alcohol, polysorbate 60, cetyl alcohol, benzyl alcohol, glycerin, sorbitan monostearate, methylparaben, and propylparaben), and further containing white petroleum and xanthan gum (column 18, lines 35-53, of Skwierczynski). The viscosity of Formula A is 33,000 cps, clearly much greater than the less than 100 cps viscosity required by Applicant's claims. Formulation B is a new and novel formulation having a higher viscosity (64,000 cps) than Formulation A (column 29, lines 1-15, of Skwierczynski). Formulation B does not contain xanthan gum. Skwierczynski finds "[d]ue to the higher viscosity of Formulation B, intravaginal administration to the rats was considerably easier and retention of Formulation B was superior to Formulation A" (column 20, lines 56-59, of Skwierczynski). Skwierczynski further states that the rate and extent of absorption of the immune response modifier was greater for Formulation B than for Formulation A (column 20, line 60 to column 21, line 3, of Skwierczynski). Thus the combinations of Crooks and Skwierczynski or Miller and Skwierczynski do not provide guidance or motivation to one of ordinary skill in the art to create lower viscosity nasal sprayable compositions with a reasonable expectation of success.

The Examiner admits that Skwierczynski was not used for its viscosity teaching. However, neither Crooks nor Miller teach compositions with viscosities of less than 100 cps. The Examiner,

therefore, has not created a *prima facie* case for obviousness of the limitation of a viscosity of less than 100 cps. The Examiner attempts to argue that such a property is a characteristic property of the compositions; however, the only compositions in the cited art that recite the inclusion of a viscosity enhancer or xanthan gum have viscosities greater than 100 cps. Thus it is unclear how the claimed viscosity is an inherent property of any composition suggested by the cited art. It is further unclear how one skilled in the art would reasonably expect success in creating and delivering such a composition when the prior art recites improved administration through higher viscosity formulations.

Applicant submits the Examiner supplies no motivation to combine Crooks or Miller with Skwierczynski to arrive at a less viscous, sprayable formulation as presently claimed, and that Skwierczynski provides no reasonable expectation of success for such a composition. One skilled in the art, guided by Skwierczynski, would seek to improve upon the superior Formulation B in order to provide a highly viscous non-sprayable formulation. Also, since Formulation B does not include xanthan gum, one skilled in the art would not be motivated to use this ingredient.

Applicant further submits that one skilled in the art, aware of the combined teachings of Crooks, Miller, and Skwierczynski, would not be led to the claimed invention. As discussed above, neither Crooks, Miller, nor Skwierczynski teach a sprayable formulation having a viscosity of less than 100 cps for nasal delivery. Crooks only very generally teaches that an immune response modifier may be conventionally formulated. The combination of Miller and Skwierczynski teach that topical formulations with higher viscosity, such as the Formulation B of Skwierczynski, are more desirable in order to enhance the residence time of the immune response modifier on the mucosal membrane of the vagina or cervix. Therefore, the cited art does not provide one of ordinary skill the direction to formulate, with a reasonable expectation of success, the invention as claimed. Rather, the cited art, taken as a whole, teaches that a higher viscosity formulation is better than a lower viscosity formulation. One skilled in the art, seeking to develop a formulation for nasal delivery, would certainly not be led to develop a sprayable formulation for nasal delivery having a viscosity of less than 100 cps as is claimed based on the cited art.

In light of the present Amendment and above Remarks, Applicant submits that presently amended claims 1-7, 11, 12, 15-21, 35, and 49 are not obvious over Crooks and Miller in view of Skwierczynski. Applicant respectfully requests this rejection under § 103 be withdrawn.

In view of the above Amendment and Remarks, Applicant believes the pending Application is in condition for allowance.

Applicant believes no fee is due with this Amendment. However, if a fee is due, please charge it to our Deposit Account No. 23/2825, under Docket No. C1271.70077US00, from which the undersigned is authorized to draw.

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Respectfully submitted,

By /C. Hunter Baker/

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